Vaccine Efficacy

How vaccines provide protection against disease

BY DR. STACEY OKE
ANNE M. EBERHARDT PHOTOS

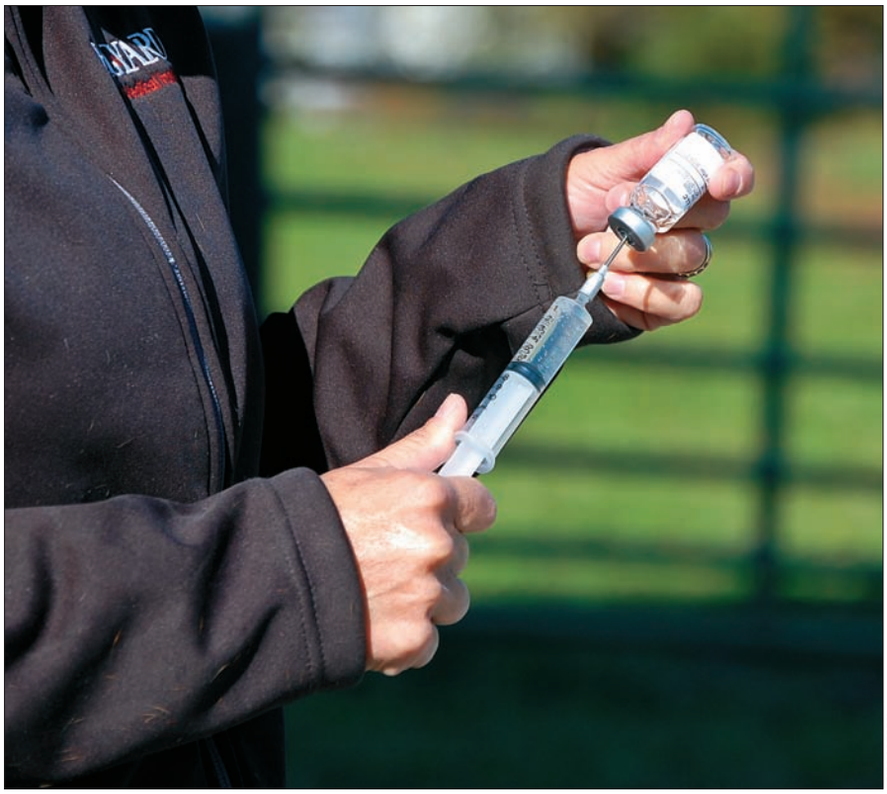
Most of us have received vaccinations or "shots," and most of us have watched our horses get theirs, but how many of us really understand how these vaccines work? Why are some vaccines administered annually whereas others are administered more frequently in at-risk horses? How do these vaccines provide protection against disease?

In an attempt to answer these questions, let's begin with a basic explanation of how a horse's immune system works and responds to invading disease-causing microorganisms (i.e., bacterial, viral, and parasitic pathogens [organisms that cause disease]).

Immune System Basics

Cells in a mammal's body are microscopic elements containing a complete set of genetic material (DNA) and a variety of organelles (specialized structures within a cell) that produce energy for the cell to function. Even microscopic organisms such as viruses and bacteria or larger disease-causing parasites contain genetic material enclosed within a membrane or envelope. These organisms have antigens—structures or molecules that induce an immune reaction. Antigens are like flags that tell a mammal's immune system that a "foreign" and potentially dangerous material is present (picture the classic skull and crossbones flag on a pirate ship). The immune system tracks down the antigens (such as those on the surface of a pathogenic bacterium or virus, for example) and does everything it can to neutralize and destroy the invading organisms.

There are two main classes of cells the immune system uses to fight invading pathogens: B cells and T cells. Once B cells recognize a nonself antigen, they begin producing antibodies (special infection-fighting proteins) that cover the antigens on the surface of the viruses, bacteria, parasites, fungi, or toxin (in the case of tetanus). These antibodies signal other immune system cells to come destroy the invading organism, leaving little to no trace that it was ever there. B cells are most effective for destroying microorganisms that are easily "seen" by the horse's immune system. Some microbes, such as *Rhodococcus equi, Salmonella*, or *Babesia caballi* (one of the causative agents of equine piroplasmosis), live inside the horse's cells (e.g., inside red blood cells) and can therefore hide from B cells. In these cases the horse's immune system recruits T cells, including helper T cells and killer T cells, to fight off the infection-causing microorganisms.



ERICA LARSON

Equine vaccines are usually prepared in liquid form and administered via injection

What Is a Vaccine?

A vaccine is a medically prepared product intended to stimulate active protection against disease. In essence, a vaccine tricks the horse's immune system into thinking that a pathogenic virus or bacterium is attempting to infect the horse. That is, vaccines stimulate the appropriate B and T cells into action, and these cells subsequently "memorize" the particular pathogen so that should the same microorganism attempt to infect the vaccinated horse in the future, the B or T cells will kill it rapidly. The end result is that a vaccinated horse still gets infected if exposed to the organism, but he either fights off the infection without showing any signs of illness, or the severity and duration of disease are markedly decreased. In contrast, an unvaccinated horse will need to start an immune response from scratch and experience some signs of illness until the immune system kicks in and responds to the invading pathogen with the appropriate immune response.

There are different types of vaccines. Some contain the whole, killed microorganism, whereas others contain live microorganisms that have been modified so they are not pathogenic but will still cause the horse's immune system to mount an immune response.

Equine vaccines are usually prepared in liquid form and are most commonly administered via an injection (e.g., rabies, tetanus) or sprayed intranasally (e.g., one type of strangles vaccine and one influenza virus vaccine are sprayed into a nostril).

Duration of Immunity

How long a vaccine's effects last dictates how frequently a horse needs to be revaccinated. Some vaccines are estimated to stimulate a long duration of

immunity. For example, the rabies vaccine for horses manufactured by Merial (Imrab 3) is administered once yearly in adult horses. In contrast, equine influenza vaccines given intramuscularly are administered at least every six months in at-risk horses. Part of the reason this intramuscular influenza vaccine must be administered more frequently is that the immune response it generates is not the same as the response generated after a natural infection. Horses normally become infected by inhaling the virus, and the immune cells in the membranes lining the nasal passages and upper respiratory tract play an important part in fighting the infection. Influenza vaccines injected intramuscularly stimulate a different part of the immune system than an intranasal influenza vaccine that targets the nasal mucosa.

In addition, the exact duration of immunity varies from horse to horse and depends on how each horse's immune system responds to vaccination and such factors as intercurrent disease (a disease, such as equine Cushing's disease, that occurs during the course of another disease process).

What Does Your Horse Need?

The list of vaccines that can be administered to horses is fairly extensive. Thankfully, not every horse needs every vaccine (otherwise record keeping would become a nightmare.).

According to Dr. D. Paul Lunn, professor of equine medicine at Colorado State University, who has lectured extensively about the equine immune system and how vaccines work, "One vaccine or vaccination program does not fit all; however, there are some general principles that owners, together with their veterinarians, can consider to help design the most appropriate program. These guidelines can help categorize vaccines as 'core,' or 'risk-based.'"

Some of the items in Lunn's guidelines include:

- Administering core vaccines (i.e., tetanus toxoid, rabies, Eastern/Western equine encephalitis, West Nile virus) to all horses;
- Vaccinating based on risk of exposure to the disease to minimize vaccine use;
- Basing vaccine selection on efficacy, not price; and
- Considering the benefits of vaccination together with the costs and risks.

"It is imperative that horse owners work with their veterinarian when establishing a vaccine protocol," Lunn said. "Together, consider the age and use of the horse, the prevalence of the disease in your area, and the season."

Vaccine Failures

As outlined in the American Association of Equine Practitioners' "Principles of Vaccination" (available free at www.AAEP.org), horse owners must be realistic in their expectations of vaccines.

"Vaccines can be excellent tools in the prevention of disease; however, vaccination by itself will not necessarily provide an absolute guarantee of preventing disease," advised Dr. Peter J. Timoney, Frederick Van Lennep Chair in Equine Veterinary Science at the University of Kentucky's Gluck Equine Research Center. Along with Lunn, Timoney was a member of the AAEP's Infectious Disease Committee that prepared the organization's vaccination guidelines in 2008.

Even in cases where veterinarians and owners have instituted state-of-the-art infection control programs, "vaccine failures" might occur because of the following reasons:

Environmental Influences Even vaccinated animals can be exposed to high enough doses of infectious agents to overcome their immune systems defenses.

Stress, overcrowding, parasitism, poor nutrition, poor sanitation, lack of a clean source of water, intercurrent diseases, lack of insect and small rodent control, and lack of appropriate biosecurity measures all can increase the risk of infectious disease spread, even among vaccinated horses.

"Unless other infectious disease control measures such as sound systems of management and biosecurity are implemented on a farm, vaccines alone may not necessarily protect a horse from disease," Timoney said. "Good managerial practices are also needed as a complement to sound vaccination policies to maximize the health of the horse and enable it to fight off pathogens."

Improper Timing Another reason vaccines can potentially fail is if the horse is not vaccinated in enough time to mount an appropriate immune response prior to pathogen exposure.

"It can take 10 to 14 days for the immune system's B cells to make antibodies against the pathogen in the vaccine," Timoney explained. "Horses therefore need to be vaccinated approximately two to three weeks before exposure if a vaccine can be expected to work."

If, for example, you know your horse is going to be shipped to a farm or a training facility with a large number of other horses, then vaccinate in advance of this event. Unvaccinated horses might require an initial "priming" in which two doses of the vaccine must be administered separated by a two-to-four week period prior to potential exposure. In these cases the horse will need to be vaccinated even further in advance for maximal protection.

"The decision of when to vaccinate should also take into consideration the recovery time needed should an unexpected adverse reaction occur following vaccination that could interfere with the horse's performance or health during shipping," Timoney noted.

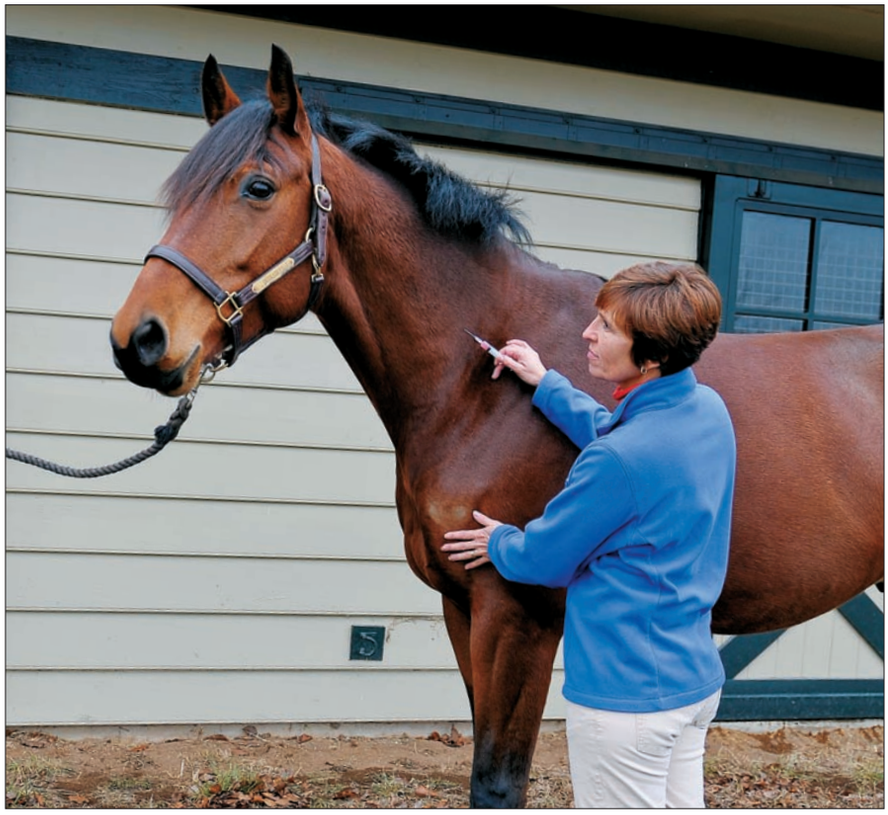
Vaccine Design Another reason for vaccine failure relates to the design of the vaccine itself.

"The immune system is complex and includes both 'innate'

responses (when it recognizes but does not adapt in response to foreign invaders) and 'adaptive' responses that include the B and T cells," Lunn said. "Only the adaptive responses of a horse's immune system can be induced by vaccination."

According to Lunn, if the vaccine doesn't sufficiently mimic the "real" infection, then the vaccine won't be effective. Take the strangles (*Streptococcus equi*) vaccination for example: Horses that get the disease often are well-protected from reinfection for considerably longer than if they were vaccinated. If vaccines could be developed that generate immunity more similar to the infection, they could be much more effective.

Antigenic Drift Pathogenic microorganisms are cunning and sly, and they try to hide from the horse's immune system. One way they do this is by antigenic drift—minor incremental changes in the antigens on the surface of pathogens. Essentially, antigenic drift changes the "flags" on the microbe's surface, making it seem like an entirely new pathogen to the horse's immune system. For example, due to antigenic drift, the antibodies that vaccinated horses have against the equine influenza virus either don't work or don't work efficiently enough to combat "new



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and improved" equine influenza viruses that have mutated their antigens.

"Vaccines are updated to deal with antigen drift, but sometimes we don't do it fast enough," added Lunn. "As the natural equine influenza virus in nature keeps evolving, over a period of years it changes sufficiently that antibody responses generated by older vaccines can't protect against the new viral strains. Generally, manufacturers are now sensitized to the concept of antigenic drift and try to keep contemporary strains in their influenza vaccines."

Adverse Events

Side effects are untoward, undesirable, and usually unanticipated events following the administration of a medical product. Adverse events are commonly mild, but on rare occasions they are serious and even life-threatening.

Mild side effects that can occur following vaccination include lethargy, fever, mild anorexia or loss of appetite, and tenderness or swelling at the administration site. Rarely, an abscess can form at the injection site. Even more rarely, clostridial myositis/myonecrosis (muscle inflammation/gas gangrene), a rapidly progressive and often fatal infection most commonly caused by the bacteria *Clostridium perfringens* and *Clostridium septicum*, can occur.

Systemic side effects can include hives, anaphylaxis (a severe allergic reaction to a component of the vaccine), or purpura hemorrhagica (immune-mediated inflammation).

"Many reactions are unpredictable, but there are ways to minimize the chance of having a reaction," Timoney advised. "For example, consider staggering the vaccine administrations to minimize the number of vaccines administered at one time."

Monitor your horse for reactions to vaccines and report all adverse reactions to your veterinarian. In turn, your veterinarian will report the reactions to the vaccine manufacturer.

If you have ever witnessed a horse react adversely to a medication—not just vaccines but antibiotics, sedatives, or other drugs—it can be a disturbing and emotionally charged experience. It is important to recognize that any medication can potentially cause an adverse reaction. Luckily, these reactions are most often mild, and the horse should recover within a few minutes to hours, without any form of veterinary intervention. All told, the benefits of vaccination far outweigh the risks, especially for the core vaccines.

Take-Home Message

Always discuss the pros and cons of vaccinating against one or more diseases with your veterinarian, and devise a vaccine plan that works best for your equine operation. Although the AAEP has a list of "recommended" vaccines for horses, each horse or farm has different vaccination needs. Also, revisit your plan each year to ensure the horses are maximally protected.

Excerpted from The Horse: Your Guide to Equine Health Care. Free weekly newsletters at *www.TheHorse.com*

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YOUR GUIDE TO EQUINE HEALTH CARE